

Appln. No. 09/050,249  
Amd. dated November 3, 2003  
Reply to Office Action of May 20, 2003

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-92 (Cancelled)

93 (Currently amended). A monoclonal antibody which specifically recognizes (i) IGIF or IL-18 having the following physiochemical properties of (1) to (4), or (ii) a variant thereof which has the same antigenic fragment(s) as in (i) to be used in obtaining said monoclonal antibody, has the physicochemical properties of (1) to (3), ~~as the protein of (i)~~ and has an amino acid sequence of SEQ ID NO:2 in which one or more amino acids are replaced with different amino acids, one or more amino acids are added to the N- or C-terminus of SEQ ID NO:2, or one or more amino acids at the N- or C-terminus of SEQ ID NO:2 are deleted:

- (1) Molecular weight  
19,000±5,000 daltons on gel filtration and sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE);
- (2) Isoelectric point (pI)  
4.8±1.0 on chromatofocusing;
- (3) Biological activity

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Inducing the interferon- $\gamma$  production by  
immunocompetent cells; and

(4) Amino acid sequence

~~comprising~~ Comprising the amino acid sequence of  
SEQ ID NO:2, wherein Xaa is Met or Thr.

94 (Currently amended). A monoclonal antibody  
according to claim 93, wherein the amino acid sequence of the  
IGIF or IL-18 is encoded by a cDNA which hybridizes with a probe  
having the coding sequence shown in SEQ ID NO:1 at 60°C in a  
solution of 5 x SSPE, 5 x Denhardt's solution, 0.5% (w/v) sodium  
dodecyl sulfate (SDS), and 100  $\mu$ g/ml denatured salmon sperm DNA  
~~and after washing in 6xSSC.~~

95 (Previously presented). A monoclonal antibody  
according to claim 93, wherein said IGIF or IL-18 is obtainable  
from a mammal.

96 (Previously presented). A monoclonal antibody  
according to claim 93, wherein the IGIF or IL-18 comprises the  
amino acid sequence shown as residues 26-43 and 79-103 of SEQ ID  
NO:2.

97 (Previously presented). A monoclonal antibody which  
specifically recognizes a polypeptide having the amino acid  
sequence shown in SEQ ID NO:2, wherein Xaa is Met or Thr.

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98(Previously presented). A monoclonal antibody according to any one of claims 93 to 97 which is an IgG or IgM class antibody.

99(Previously presented). An antibody according to any one of claims 93 to 97 which is labeled with a radiolabel, an enzyme, or a fluorophore.

100(Previously presented). An antibody according to any one of claims 93 to 97 which is capable of inhibiting the biological activity of IGIF or IL-18.

101(Previously presented). A hybridoma which produces a monoclonal antibody according to any one of claims 93 to 97.

102(Previously presented). A method for producing a monoclonal antibody which comprises culturing a hybridoma according to claim 101 *in vitro* or *in vivo* under conditions suitable to promote production of the antibody and recovering the antibody so produced.

103(Currently amended). A method according to claim 102, further comprising the step of subjecting the antibody to one or more processes selected from the group consisting of salting out, dialysis, filtration, concentration, centrifugation, separatory sedimentation, gel filtration chromatography, ion-

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exchange chromatography, HPLC, affinity chromatography, gel electrophoresis, and isoelectric focusing.

104 (Previously presented). A method for determining the presence of IGIF or IL-18 in a sample, comprising the steps of:

contacting a sample suspected to contain IGIF or IL-18 with an antibody according to any one of claims 93 to 97 under conditions suitable to promote the specific binding of the antibody to IGIF or IL-18 to form an immune complex; and detecting any such immune complex which is so formed.

105 (Previously presented). A method according to claim 104, wherein the antibody is immobilized on an insoluble matrix or substrate.

106 (Previously presented). A method according to claim 104, wherein the antibody is labeled with a radiolabel, an enzyme, or a fluoprophore.

107 (Previously presented). A method according to claim 104, further comprising the step of quantifying the amount of IGIF or IL-18 present in the sample.

108 (Previously presented). A method according to claim 104, wherein the IGIF or IL-18 has the amino acid sequence shown in SEQ ID NO:2, wherein Xaa is Met or Thr.

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109(Previously presented). A method for purifying IGIF or IL-18 from a sample containing other components, comprising the steps of:

contacting the sample with a monoclonal antibody according to any one of claims 93 to 97 under conditions suitable to promote the specific binding of the antibody to IGIF or IL-18 to form an immune complex; and

separating the immune complex from at least one of the other components in the sample.

110(Previously presented). A method according to claim 109, further comprising the step of recovering the IGIF or IL-18 from the immune complex.

111(Previously presented). A method according to claim 109, wherein the antibody is immobilized on an insoluble matrix.

112(Previously presented). A method according to claim 109, wherein the contacting step is effected by applying the sample to a chromatography column comprising an insoluble matrix.

113(Previously presented). A method according to claim 112, further comprising the step of recovering the IGIF or IL-18 from the chromatography column.

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114(Previously presented). A method according to claim 113, wherein the IGIF or IL-18 is recovered in nearly quantitative yield and with a purity of at least 95%.

115(Previously presented). A method according to claim 109, wherein the IGIF or IL-18 has the amino acid sequence shown in SEQ ID NO:2, wherein Xaa is Met or Thr.

116(Previously presented). A method of inhibiting the biological activity of IGIF or IL-18, comprising the step of contacting an antibody according to claim 100, with the IGIF or IL-18.

117(Previously presented). A method according to claim 116, wherein the IGIF or IL-18 has the amino acid sequence shown in SEQ ID NO:2, wherein Xaa is Met or Thr.

118(Previously presented)). A monoclonal antibody specific to interferon-gamma (IFN- $\gamma$ ) inducing protein, also known as IGIF and IL-18.

119(Previously presented). A monoclonal antibody according to claim 95, wherein said mammal is mouse.

120(Currently amended). An antibody obtainable by using, as an antigen (i) IGIF or IL-18 having the following

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physiochemical properties of (1) to (4), or (ii) an antigenic fragment of said IGIF or IL-18:

- (1) Molecular weight  
19,000 $\pm$ 5,000 daltons on gel filtration and sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE);
- (2) Isoelectric point (pI)  
4.8 $\pm$ 1.0 on chromatofocusing;
- (3) Biological activity  
Inducing interferon- $\gamma$  production by immunocompetent cells; and
- (4) Amino acid sequence  
Comprising the amino acid sequence of SEQ ID NO:2, wherein Xaa is Met or Thr.